

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/GB2004/001428

International filing date (day/month/year)
01.04.2004

Priority date (day/month/year)
01.04.2003

International Patent Classification (IPC) or both national classification and IPC
A61K38/00, A61K38/17, A61P29/00, A61P37/00, A61P37/08, A61P27/14, A61P17/06

Applicant
EVOLUTEC LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/001428

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
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Box No. II Priority

1. ☒ The following document has not been furnished:

☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
☒ claims Nos. 1-10 (in part) as well as 1-9 in respect to industrial applicability

because:

- ☒ the said international application, or the said claims Nos. 1-9 in respect to industrial applicability relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the whole application or for said claims Nos. 1-10 (in part)
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
- | | |
|----------------------------|--|
| the written form | <input type="checkbox"/> has not been furnished |
| | <input type="checkbox"/> does not comply with the standard |
| the computer readable form | <input type="checkbox"/> has not been furnished |
| | <input type="checkbox"/> does not comply with the standard |
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/001428

Box No. V Reasoned statement under Rule 43b/s.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	-
	No: Claims	1-10
Inventive step (IS)	Yes: Claims	-
	No: Claims	1-10
Industrial applicability (IA)	Yes: Claims	10
	No: Claims	-

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Claims 1-9 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).
2. Since the search has only been carried out for those parts which appear to be clear, supported and disclosed, namely relating to the compounds as defined in claims 8 and 9 and the diseases as defined in claims 2 and 3, the following claims are in part not subject of the international preliminary examination: claims 1-10.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. The following documents are referred to in this communication:

- D1: WO 01/15719 A (NUTTALL PATRICIA ANNE ; PAESEN GUIDO CHRISTIAAN (GB); EVOLUTEC LTD (GB) 8 March 2001 (2001-03-08)
- D2: WO 01/40469 A (UNIV YALE) 7 June 2001 (2001-06-07)
- D3: WO 99/27104 A (OXFORD VACS LTD ; NUTTALL PATRICIA ANN (GB); PAESEN GUIDO CHRISTIAN (G) 3 June 1999 (1999-06-03)

2. Novelty

D1 claims the use of histacalin proteins which are the same as the proteins mentioned in the present application (eg. EV131) for the treatment of any conjunctivitis, more preferably allergic conjunctivitis. In particular, seasonal and perennial conjunctivitis, as well as vernal keratoconjunctivitis, giant papillary conjunctivitis and atopic keratoconjunctivitis. Hence, claims 1-10 cannot be regarded as novel.

Tick polypeptides are claimed in D2 whereby one of these, Salp25D, possesses histamine-binding motifs and is useful to treat conditions characterized by the production of histamine. Such conditions include, but are not limited to, hayfever, allergic reactions,

respiratory infections, and others. Other proteins cited are useful in the treatment of autoimmune diseases, including lupus, arthritis and diabetes, and tissue and organ transplant rejection, as well as atherosclerosis. Claims 1-8 and 10 are not novel in view of D2.

D3 claims histamine or serotonin binding compounds capable of binding to histamine or serotonin with a dissociation constant of less than $10^{-7}M$ and known as FS-HBP1, FS-HBP2, MS-HBP and D.RET6. The use as anti-inflammatory drugs and the treatment of allergies also are claimed rendering claims 1,2, and 4-10 not novel.

3. Inventive step

The document D3 is regarded as being the closest prior art to the subject-matter of claims 1-10.

The subject-matter of claims 1-10 therefore differs from D3 in that the specific diseases cited in claim 3 of the present application are not mentioned in D3.

The problem to be solved by the present invention may therefore be regarded as finding other applications, ie. diseases, where the mentioned histamine binding compounds can be used in order to treat them.

In case of novelty the following applies:

The solution proposed in claims 1-10 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons.

It is already known to use the specific histamine binding compounds claimed for the same conditions, namely allergic, inflammatory, and auto-immune conditions from D1-D3. Specific diseases such as conjunctivitis, lupus and atherosclerosis also have been disclosed (D1, D2).

The other diseases cited in claim 3 such as "ARDS", "psoriasis", "ulcerative colitis" and others are merely obvious possibilities of inflammatory, allergic, and auto-immune diseases where the skilled person would apply the known compounds in order to treat them since it is known that any such condition can be treated by the above mentioned proteins.

In addition, it has to be remarked that apart from an immune complex model in the mouse, the description only contains examples showing the effects of EV131 in endotoxin-induced

bronchoconstriction in a murine model for the investigation of its utility in allergic asthma as well as a study related to allergic conjunctivitis.

4. For the assessment of the present claims 1-9 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VII

Certain defects in the international application

Claim 8 contains references to the description, namely references to prior art. According to Rule 6.2(a) PCT, claims should not contain such references except where absolutely necessary, which is not the case here.

Re Item VIII

Certain observations on the international application

1. Claims 1-10 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claims attempt to define the subject-matter by reference to a desirable characteristic or in terms of the result to be achieved, which merely amounts to a statement of the underlying problem, without providing the technical features necessary for achieving this result, namely (a) the disease condition by defining it as being mediated by neutrophil cells, and (b) the compounds by defining them as being binding to histamine.

2. Claim 5 is unclear in comparison to the other claims and in regard to the dissociation constant of greater than 10^{-7} M since for all the claimed proteins the contrary, namely a dissociation constant of less than 10^{-7} M is required.